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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,717	05/16/2001	Nabil Hanna	P 0280623 1999-30-0466CP2	9413

909 7590 06/29/2004

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,717	HANNA ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-81* is/are pending in the application.

4a) Of the above claim(s) *6,18,19,31,40-56,66,67,70 and 71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7-17, 20-30, 32-39, 57-65, 68, 69, 72-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 3/2/04, has been entered.
Claims 7, 10, 11-13, 21, 24, 26, 31, 33, 35 have been amended.
Claims 82-103 have been canceled.

Applicant's election of the combination of anti-CD40L antibody and anti-CD20 antibody, the radiolabel ytrrium 90, the chemotherapeutic CHOP and non-Hodgkin's disease as the B cell lymphoma in Paper No. 8, filed 3/11/03, with traverse has been ackno.

Claims 6, 18, 19, 31, 40, 41, 66, 67, 70 and 71 have been withdrawn as being drawn to nonelected inventions / species.

Previously, claims 42-56 have been withdrawn from consideration by the examiner, as being drawn to nonelected Invention.

Claims 1-5, 7-17, 20-30, 32-39, 57-65, 68, 69 and 72-81 are under consideration in the instant application as they read on the elected species.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's amendment, filed 3/2/04.
The rejections of record can be found in the previous Office Action.

3. Claims 7, 8, 21, 33, 35, 63, 69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Claims 7, 8, 21, 33, 35, 63, 69: It is apparent that IDEC-131, 3E4, 2H5, 2H8, 4D9-8, 4D9-9, 24-31, 24-43, 89-76 or 89-79 as well as the RITUXAN and B1 antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent cell lines / hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

Applicant's arguments and Exhibits, filed 3/2/04, have been fully considered but are not clear with respect to the conditions required for the deposit of biological materials under 35 USC 112, first paragraph.

Applicant is reminded that in addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

It is not clear from applicant's evidence from the ATCC whether they are any restrictions on the claimed antibodies.

In addition, the data sheet for the anti-CD40L 24-31 clone indicates that the antibody is for in vitro research use only and nor for use in or on humans or animals or for diagnostics.

Although applicant relies upon the availability of "a" B1 antibody from Coulter as disclosed in U.S. Patent No. 6,565,827, there is insufficient objective evidence concerning the conditions for such availability.

Applicant is reminded of the following as well.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Again, it is noted that certain of these antibodies are claimed in U.S. Patents (e.g. see art rejections below) which would be indicative, but not necessarily mean (see MPEP 2404.01) that the enablement of biological materials under 35 USC, 112, first paragraph, has been satisfied.

Applicant is required to indicate which antibodies are enabled accordingly and to satisfy the deposit of the biological materials for the others accordingly.

4. Claims 7, 8, 11-13, 21, 33, 35, 63 and 69 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7, 8, 21, 33, 35, 63, 69: 24-31, rituximab, 2B8 and B1 are indefinite in the recitation of these "designations" because their characteristics are not known. The use of these "designations" as the sole means of identifying the claimed antibodies renders the claims indefinite because these are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same laboratory designations to define completely distinct cell lines .

Amending the claims to recite the appropriate ATCC Accession Numbers would obviate this rejection.

Applicant's reliance upon the disclosures of U.S. Patents as well as the letter from the U.S. Adopted Names Council is acknowledged. However, this rejections is set forth to make the record clear that these designations read on a specific biological material. In the absence of the appropriate deposit accession number, the metes and bounds of these antibody designations are not necessarily specific to a particular biological material. Even USAN letter indicates that rituximab (which is not readily apparent in the specification as filed) refers to IDEC-C2B8 and IDEC-102.

Again, amending the claims to recite the appropriate ATCC Accession Numbers would obviate this rejection

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

5. Claims 1-5, 7-17, 20-30, 32-39, 57-65, 68, 69 and 72-81 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kaminski et al. (U.S. Patent No. 6,287,537) AND/OR Anderson et al. (U.S. Patent No. 5,843,439) in
view of Gruss et al. (Leukemia and Lymphoma 24: 393-422, 1997), Carbone et al. (Am. J. Pathol. 147: 912-922, 1995), Black et al. (U.S. Patent No. 6,001,358), in view of standard chemotherapeutic treatments, including combination therapy of malignancies, including lymphomas known and practiced by the ordinary artisan at the time the invention was made, as acknowledged on pages 24-28 of the instant specification for the reasons of record.

Applicant's arguments in conjunction with the Hariharan declaration under 37 C.F.R. § 1.132, filed 3/2/04, have been fully considered but are not found convincing essentially for the reasons of record.

With respect to the asserted lack of clarity as to which reference(s) applies to which claim(s), the primary references are in the alternative and each primary reference can be combined with the secondary teachings.

While applicant noted that Kaminiski and Anderson are directed to the use of anti-CD20 anitbodies for cancer therapy and that claim 1 is directed toward anti-CD40L therapies, applicant is reminded that applicant has elected the combination of anti-CD40L antibody and anti-CD20 antibody, the radiolabel ytrrium 90, the chemotherapeutic CHOP and non-Hodgkin's disease as the B cell lymphoma in Paper No. 8, filed 3/11/03.

In addition, applicant argues in conjunction with the Hariharan declaration under 37 C.F.R. § 1.132 that the prior art alone or in combination do not describe, suggest or motivate blockade of CD40/CD40L signaling in malignant B cell by administering anti-CD40L antibody antagonists.

While applicant acknowledges that Carbone proposes that CD40/CD40L signaling in malignant cells, applicant notes that Carbone states that the functional significance of the expression of CD40L on reactive T lymphocytes deserves speculation. Applicant asserts that expression data merely invites experimentation to determine protein function in those cells where it is expressed.

Applicant argues that Gruss actually teaches away from the claimed invention, given that Gruss describes inhibition of B cell proliferation in the presence of recombinant CD40L and suggests a role for CD40/CD40L signaling in malignant cells which is directly opposite to that described in the present application. Applicant asserts that Gruss suggests that activation of CD40/CD40L signaling may be a viable therapy for B cell malignancies.

In contrast to Gruss, applicant asserts that the present invention is directed to blockade of cD40/CD40L signaling for treatment of B cell malignancies.

While it is noted that Gruss et al. does teach the anti-proliferative and pro-apoptotic effects of recombinant CD40L on high grade B-NHLs as an appealing biologic approach for treatment of these neoplasms (page 405, column 1), Gruss et al. does teach conflicting results with the role of CD40:CD40L triggering of neoplastic B cells, including the ability of CD40 triggering to rescue neoplastic B CLL (see pages 404-405, overlapping paragraph). Here, it is noted that one possible explanation for these conflicting results is the type of cell lines utilized for these studies. In discussing B cell lymphomas and lymphoproliferative disorders, it is noted that engagement of CD40 by most tumor B cells in vitro results in efficient transduction of signals promoting cell activation and proliferations (see pages 404-405, B cell Lymphomas and Lymphoproliferative Disorders, particularly page 404, column 2, paragraph 1).

Therefore, the prior art of Carbone et al. and Gruss et al. taught the importance of CD40L-mediated interactions in B cell non-Hodgkin's lymphoma and clinical manifestations of lymphoma growth and therapeutic intervention. Also as pointed out above, Gruss et al. does teach that CD40:CD40L interactions are part of cellular activation and neoplastic tumor cell growth which would be useful for the therapeutic management of $CD40^+$ tumors (see page 404, column 1).

Given the teachings of Kaminksi et al. to employ radiolabeled antibodies in combination with other treatments to treat leukemia as well as the acknowledgment by applicant that combination therapy was known and practiced in the art at the time the invention was made, one of ordinary skill in the art would have been motivated to treat B cell leukemia with a combination of therapies.

Given the expression of CD20 and CD40 and the ability of activation via CD20 and/or CD40, the ordinary artisan would have been motivated to target B cell non-Hodgkin's lymphoma directly with radiolabeled CD20-specific antibodies and to diminish activation of said B cell leukemia by blocking activation by CD40 ligand expressing T cells with CD40L-specific antibodies.

One of ordinary skill in the art would have employed non-radiolabeled CD40L-specific antibodies, given the expression of CD40L on normal activated T cells and the role of such CD40L on such T cells to stimulate CD40-expressing B cell lymphoma cells, as taught above.

Given the standard regimen of chemotherapy in leukemic patients and the teachings of Kaminski et al. to combine standard therapy with radiolabeled antibodies, one of ordinary skill in the art at the time the invention was made to employ multiple modalities to treat B cell lymphomas. Given the addition of non-radiolabeled CD40L-specific antibodies, the ordinary artisan would have been administering a less toxic therapeutic regimen, when compared to radiolabeled antibodies and chemotherapeutic agents.

One of ordinary skill in the art at the time the invention was made would have been motivated to select radiolabeled CD20-specific antibodies, non-radiolabeled CD40L-specific antibodies and standard chemotherapeutic to treat B cell lymphomas at the time the invention was made, given the teachings above. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

6. Claims 1-3, 9-14 and 16-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over pending claims of copending applications USSNs 09/435,992 and 09/772,938. Given the election in the instant case, the conflicting claims may or may not be identical, depending upon the invention(s) elected in these copending applications. The claims are not patentably distinct from each other because they appear to read on treating the same or nearly the same reagents to treat the same or nearly the same (leukemias and) lymphomas with the same or nearly the same anti-CD40L and anti-CD20 antibodies.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's amendment, filed 3/2/04, notes that terminal disclaimer may be iled if the rejection still stands when one or more claims in the istant application are in condition for allowance.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9.. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
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June 25, 2004